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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,490	04/06/2001	Elizabeth S. Stuart	08952-008001 / UMA 00-19	5744

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,490	STUART ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,10 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,10 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This Office Action is responsive to Applicant's response filed on August 7, 2006. Claims 1-6 and 11-17 have been cancelled. Claims, 7, 9-10 and 18-20 are pending and under examination.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejections Maintained

3. The rejection under 35 U.S.C. 103(a) is maintained for claims 7, 9, and 18-20 for the reasons set forth on pages 3-6 paragraph 3 of the previous Office Action.

The rejection was on the grounds that Whittum-Hudson et al teach that the chlamydial exoglycolipid antigen (GLXA) is expressed at all differentiation stages of the *Chlamydia* organism and is secreted from infected cells (page 1116, 2nd column). Whittum-Hudson et al teach that antigenic determinants of GLXA reside on its polysaccharide component (GLXA oligosaccharide)(page 1116).

Whittum-Hudson et al and Stuart et al do not teach the monoclonal antibody 89M830.

Stuart et al, 1987 teach an isolated polysaccharide component (GLXA oligosaccharide) (pages 527-530). Stuart et al, 1987 teach that the polysaccharide component is antigenic (page 527).

Stuart et al, 1994 teach that the epitope on the polysaccharide component is recognized and binds to the monoclonal antibody 89MS30 (page 89).

Whittum-Hudson et al ,Stuart et al, 1987, Stuart et al, 1994 and do not teach that the GLXA oligosaccharide is couple to a carrier molecule.

Dick, Jr. et al teach conjugation of bacterial carbohydrate (polysaccharide) antigens to a carrier protein. Dick, Jr. et al teach that some subjects (e.g. children under 18 months and elderly people) fail to produce antibodies when stimulated with capsular polysaccharide immunogens (CPS) at level too low to be protective (page 49). Dick, Jr. et al teach that high-risk populations retain the ability to produce protective antibodies against immunogenic proteins such as diphtheria toxoid or tetanus toxoid by a process that can be adapted to carbohydrate antigens (page 49). Dick, Jr. et al teach that proteins and polysaccharides are classified into two separate classes of antigens

thymus dependent (TD) and thymus independent (TI) antigens, respectively (page 49). Dick et al teach that polysaccharides classified as TI antigens have multiple repeat epitopes on their polymeric chains which collectively bind and cross-link immunoglobulin receptors on the surface of B cells and the net effect is the induction of cellular differentiation processes that yield antibody-producing plasma cells (page 49). Dick, Jr. et al teach that it is well established that covalent bonding of carbohydrate antigens to proteins can transform the carbohydrate into the status of a TD antigen (pages 49 and 56). Dick, Jr. et al teach that CPS can be linked to carrier proteins directly or by bifunctional linkers (spacer arms) (pages 71-72) which overcome conjugation limitations imposed by steric effects (page 71). Dick, Jr. et al teach that linkers can promote improved antigenicity for the bound components as compared to results obtained when testing the same antigens conjugated by a direct method (page 72). Dick, Jr. et al teach that spacers (i.e. linkers) permit corresponding increases in translational and rotational characteristics of the antigens, increasing access of the binding sites to soluble antigens (page 72). Dick, Jr. et al teach that linkers can be covalently bound to carbohydrate components (page 70).

It would be *prima facie* obvious at the time the invention was made to use covalently couple the oligosaccharide/polysaccharide of chlamydial GLXA as taught by the combined prior art references (Whittum-Hudson et al and Stuart et al , 1987 to a carrier protein (e.g. diphtheria toxoid or tetanus toxoid) as taught by Dick, Jr. et al because Whittum-Hudson et al teach that antigenic determinants of GLXA reside on its polysaccharide component, making it an T-independent antigen and GXLA would not be expected to generate protective IgG antibody response or T helper cell responses and Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins thereby, demonstrating a thymus dependent (TD) response to carbohydrate components and enhancing the immune response to carbohydrate component. It would be expected barring evidence to the contrary, a composition comprising GLXA covalently coupled to a carrier protein would be effective in stimulating a response from the immune system since the polysaccharide component has been demonstrated to be antigenic. One of skill in the art would have been motivated to produce the immunogen as combined above because Stuart et al, 1987 teach that GLXA polysaccharide is antigenic and suggest that it is reasonable to assume that soluble antigens may play a role in the immunopathology associated with diseases caused by *Chlamydia* (page 533). Additionally, Dick, Jr. et al teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table I. Dick, Jr. et al disclose properties of glycoconjugate vaccines as well as design choices that must be consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

Applicant's Arguments

A) Applicant urges that a *prima facie* case of obviousness has not been established. Applicant urges that the prior art fails to teach or suggest the claimed elements. Applicant urges that the cited reference alone or in combination do not teach covalently coupling one or more isolated GLXA oligosaccharides to a carrier group. Applicant urges that the two cited reference teach away from the claimed invention. Applicant urges that Whittum-Hudson et al teach whole GLXA to conduct its studies. The reference does not teach isolated GLXA oligosaccharides. Applicant urges that Stuart et al, 1987 teach a polysaccharide component and the reference does not suggest isolating GLXA oligosaccharides and coupling them to a carrier group. Stuart et al, 1987 discloses that both the lipid and polysaccharides are antigenic. Stuart et al, 1987 fail to lead the skilled practitioner to isolated oligosaccharides. Applicant urges that Stuart et al, 1994 discloses whole GLXA and not isolated oligosaccharides from GLXA. Stuart et al, 1994, does not indicate that the 89MS30 recognizes the polysaccharide component of GLXA. Applicant urges that Dick, Jr.et al discloses preparation of glycoconjugates of carbohydrates from capsular and lipopolysacchrides. Dick,Jr. et al fail to offer any teaching or suggestion about GLXA or any other secreted glycolipids coupled to carriers.

B) Applicant urges that the cited reference fail to provide motivation or suggestion to combine the references.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed August 7, 2006 have been fully considered but they are not persuasive.

A) In response to applicant's argument that no case of prima facie obviousness has been established, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Stuart et al teach isolated GLXA polysaccharides or oligosaccharides. Whittum-Hudson et al disclose that the antigenic determinants of GLXA reside on the polysaccharide component. Whittum-Hudson et al also disclose that the polysaccharide component of GLXA is a T-independent antigen and would not be expected to generate protective IgG antibody responses or T helper cell responses (page 1116). However, Dick, Jr. et al teach that protein carriers can be coupled to carbohydrate components to improve antigenicity and stimulate protective antibodies. Dick, Jr. et al teach that it is well established that covalent bonding of carbohydrate antigens to proteins can transform the carbohydrate into the status of a TD antigen. Stuart et al, 1997 teach that the 89MS30 recognizes the polysaccharide component of GLXA. The prior art references do not teach away from the claimed invention.

To address Applicant's comments regarding, Whittum-Hudson et al not teaching whole GLXA, Stuart et al, 1987 not teaching coupling the polysaccharide component to a carrier and leading the practitioner to the polysaccharide or the oligosaccharide components of GLXA, it should be remembered that Applicant must not argue the reference individually, it is the combination of references that teach the claimed invention. Therefore, a case of prima facie obviousness has been established and all of the elements of the invention have been addressed by the combination prior art references.

B) To address Applicant's comments regarding motivation to combine the prior art references, as stated above the prior art references, provide an isolated oligosaccharide from GLXA (Stuart et al 1987), provides the motivation as to why the skilled artisan would be interested in the polysaccharide or oligosaccharide component (Whittum-Hudson et al), provides motivation to enhance the antigenicity of the polysaccharide component (Dick, Jr. et al), teaches that the 89MS30 antibody binds to GLXA (Stuart et al , 1994).

In view of all of the above, this rejection is maintained.

4. The rejection under 35 U.S.C. 103(a) is maintained for claims 7, 9, 10 and 18-20 for the reasons set forth on pages 6-8 paragraph 4 of the previous Office Action.

The rejection was on the grounds that the teachings of Whittum-Hudson, Stuart 1987, and Stuart 1994 and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al, Stuart 1987, Stuart, 1994 and Dick, Jr. et al as set forth supra does not teach that the linker is 2-(4-aminophenyllethylamine.

Semprevivo teaches 2-(4-aminophenyllethylamine linkers. Semprevivo teaches that oligosaccharides behave as simple haptens and must be linked either to proteins or a solid support in order to raise and isolate a specific antibody (see the Abstract). Semprevivo teaches that all oligosaccharides regardless of size become associated with the carrier protein (page 225). Semprevivo teaches that coupling oligosaccharides with a 2-(4-aminophenyllethylamine linker conserves that chemical integrity of the oligosaccharide. It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to use the 2-(4-aminophenyllethylamine linkers as taught by Semprevivo to covalently bond the carrier group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide as taught by the combined art references (Whittum- Hudson et al, Stuart, 1987, Stuart 1994, and Dick, Jr. et al) as combined above because Semprevivo has demonstrated that z-t4-aminophenyllethylamine linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of 2-(4-aminophenyllethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because 2-(4-aminophenyllethylamine teach the 2-(4-aminophenyllethylamine can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component. Dick, Jr. et al also teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table 1. Dick, Jr. et al disclose properties of glycoconjugate vaccines as well as design choices that must be taken into consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

Applicant's Arguments

Applicant urges that Semprevivo et al do not correct the deficiencies of the other cited references for the reasons articulate above. Semprevivo et al do not provide the motivation to combine the references or a reasonable expectation of success if the

references are combined. The combination would not motivated the skilled artisan to combine the references to arrive at the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed August 7, 2006 have been fully considered but they are not persuasive.

As stated above, the prior art references, provide an isolated oligosaccharide from GLXA (Stuart et al 1987), provides the motivation as to why the skilled artisan would be interested in the polysaccharide or oligosaccharide component (Whittum-Hudson et al), provides motivation to enhance the antigenicity of the polysaccharide component (Dick, Jr. et al), teaches that the 89MS30 antibody binds to GLXA (Stuart et al , 1994).

Semprevivo et al provide a teaching of the linker used to couple the polysaccharide component or the oligosaccharides to the carrier. One of ordinary skill in the art would expect success since Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component and Semprevivo et al provide such linker. It should be noted that Applicant's specification references Semprevivo et al. See page 7.

In view of all of the above, this rejection is maintained.

5. The rejection under 35 U.S.C. 103(a) is maintained for claims 7, 9, 10 and 18-20 for the reasons set forth on pages 6-8 paragraph 4 of the previous Office Action.

The rejection was on the grounds that the teachings of Whittum-Hudson, Stuart 1987, and Stuart 1994 and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al, Stuart 1987, Stuart, 1994 and Dick, Jr. et al as set forth supra does not teach that the linker is 2-(4-aminophenyllethylamine. Smith et al teach the β(p-aminophenyllethylamide (i.e. 2-(4-aminophenyllethylamine) can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Smith et al teach the coupling of oligosaccharides to bovine serum albumin and keyhole limpet hemocyanin (see the Abstract). Smith et al teach that rabbits immunized with the synthetic glycoproteins produced antibodies directed against the oligosaccharides (see the Abstract).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to use the β(p-aminophenyllethylamide (i.e. 2-(4-aminophenyllethylamine) linkers as taught by Smith et al to covalently bond the carrier group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide as taught by the prior art (Whittum-Hudson et al, Stuart, 1987, Stuart, 1994 and Dick, Jr. et al) as combined above because Smith et al have demonstrated that β-(p-aminophenyllethylamide linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of β(p-aminophenyllethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because Smith et al teach the β-(p-aminophenyllethylamide (i.e. 2-(4-aminophenyllethylamine) can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component. Dick, Jr. et al also teach that glycoconjugate vaccines directed against pathogenic bacteria are known in the art. See Table 1. Dick, Jr. et al disclose properties of glycoconjugate vaccines as well as design choices that must be taken into consideration when preparing glycoconjugate vaccines. See Tables 2 and 3.

Applicant's Arguments

Applicant urges that Smith et al do not correct the deficiencies of the other cited references for the reasons articulate above. Smith et al do not provide the motivation to combine the references or a reasonable expectation of success if the references are

combined. The combination would not motivated the skilled artisan to combine the references to arrive at the claimed invention.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed August 7, 2006 have been fully considered but they are not persuasive.

As stated above, the prior art references, provide an isolated oligosaccharide from GLXA (Stuart et al 1987), provides the motivation as to why the skilled artisan would be interested in the polysaccharide or oligosaccharide component (Whittum-Hudson et al), provides motivation to enhance the antigenicity of the polysaccharide component (Dick, Jr. et al), teaches that the 89MS30 antibody binds to GLXA (Stuart et al , 1994).

Smith et al provide a teaching of the linker used to couple the polysaccharide component or the oligosaccharides to the carrier. One of ordinary skill in the art would expect success since Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the
immune response to the response to carbohydrate component and Smith et al provide such linker.

In view of all of the above, this rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Status of Claims

6. No claims are allowed.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Albert Navarro, can be reached at (571) 272-0861.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
October 14, 2006

NITA MINNIFIELD
PRIMARY EXAMINER